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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,256	03/11/2004	Zichria Zakay-Rones	85189-5900	1732

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/800,256	ZAKAY-RONES ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,24-30,46-52,55-65* is/are pending in the application.

4a) Of the above claim(s) *6-14 and 55-65* is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *2-5,24-30 and 46-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 10/8/04 9/14/05 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/11/04,10/8/04,9/14/05*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1-14, 24-30, 46-52, and 55-65 are pending.

The cancellation of claims 15-23, 31-45, and 53-54, the amendment to claims 47-50 and 55 and the addition of claims 56-65 and the amendment to the specification filed on 9/14/05 is acknowledged by the examiner.

Election/Restrictions

Applicant's election of Group I in the reply filed on 9/14/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-14 and 55 and new claims 56-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/14/05.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/11/04, 9/14/05, and 10/8/04 are being considered by the examiner.

The international search report is considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46 and 50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 46 and 50, as best understood, are readable on a genus of a polynucleotides encoding at least one viral polypeptide, an analog or subunit thereof having oncolytic activity, wherein the genus of polynucleotides is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a genus of a polynucleotides encoding at least one viral polypeptide, an analog or subunit thereof having oncolytic activity. The specification provides sufficient description of SEQ ID NO: 1 and the fusion glycoprotein and the hemaglutinin-neuraminidase of NDV. However, the specification only describes NDV and proteins from NDV having oncolytic activity. The genus embraces DNA and RNA viruses that are not

disclosed in the instant specification. Other than NDV, the specification does not describe how to make other species embraced by the claimed invention. The specification does not disclose a structure-function correlation between NDV and the claimed genus. Thus, in view of the reasons set forth above and the numerous and complex functions of viral polypeptides, analogs or subunits, the specification does not disclose which activities of NDV correspond to the claimed genus of polynucleotides. It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of polynucleotides as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of polynucleotides that must exhibit the disclosed biological functions as contemplated by the claims.

The mere contemplation of a genus of polynucleotides encoding a viral polypeptide having oncolytic activity is not sufficient to support the present claimed invention. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of polynucleotide sequences that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction

of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of a polynucleotide sequence encoding a polypeptide, analog or subunit thereof that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 4, 5, and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention consists of a cloned NDV designated HUJ strain. Claims 4, 5, and 28-30 specifically claim the HUJ strain. Since the HUJ strain is essential to the claimed invention, it must be obtainable be a repeatable method set forth in the specification or otherwise readily available to the public. If the HUJ strain is not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of the HUJ strain. It does not appear that the HUJ strain is known and readily available or can be reproducibly made without undue

experimentation, and because claims 4, 5, and 28-30 specifically require the HUJ strain. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restriction upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request of the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

This requirement if necessary when a deposit is made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of

each member State. Amendment of the specification to recite the date of the deposit and the complete name and address of the depository is required.

It is noted that on page 11 of the specification, the applicants deposited HUJ strain with an international reference library and the strain has an assigned reference number. However, the deposit is incomplete because it does not fulfill the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 4, 5, 28, 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "HUJ strain" in claims 4, 5, and 28 is a relative term, which renders the claims indefinite. The term "HUJ strain" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of term are not defined by the instant specification because it is not apparent if the term distinguishes the NDV from a virus derived from a natural lentogenic NDV.

Claims 51 and 52 recite the limitation "the vector" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The term "pharmaceutical composition" in instant claims 2-5 and the term "unit dose" in instant claim 5 do not have patentable weight over the prior art because the terms do not distinguish the claimed invention over the prior art. See MPEP 2111-2111.02.

Instant claims 46-52 read on administering a NDV to treat cancer in a patient because NDV comprises a fusion glycoprotein and a hemaglutinin-neuraminidase glycoprotein.

The term "HUJ strain" in instant claims 4 and 28 reads on a clonal lentogenic NDV derived from a natural lentogenic NDV because the metes and bounds of the term are undefined by the instant specification and the applicants renamed a NDV derived from a natural lentogenic NDV after several passages with the term (page 11). Thus, there is nothing in the instant specification to indicate that the HUJ strain is structurally distinct from a NDV derived from lentogenic NDV.

Claims 2-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Roberts et al. (US 2003/0044384, cited on a PTO-1449). Roberts teaches a lentogenic oncolytic strain of Newcastle Disease Virus (NDV) (page 7).

Claims 2-5, 24-28, and 46-52 are rejected under 35 U.S.C. 102(e) as being anticipated by Groene et al. (US 20030077819). Groene teaches a method of treating a human with cancer comprising administering a pharmaceutical composition comprising NDV having low virulence (lentogenic) and physiologically acceptable solution (pages 1-2). Groene teaches the limitation in instant claims 25 and 26 (pages 2-3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Instant claims 46-52 read on administering a NDV to treat cancer in a patient because NDV comprises a fusion glycoprotein and a hemaglutinin-neuraminidase glycoprotein.

Claims 2-5, 24-30 and 46-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (US 2003/0044384, cited on a PTO-1449). Roberts teaches a lentogenic oncolytic strain of Newcastle Disease Virus (NDV) (page 7). Roberts teaches that there are three categories of NDV, including lentogenic NDV, which are useful (page 7). Roberts teaches a method of treating cancer in a patient using NDV (pages 8-9). Roberts teaches using several routes of administration for use in the method (pages 11-12). Roberts teaches that NDV is generally administered from about 3.times.10.sup.6 to about 5.times.10.sup.12 PFU of virus (pages 11 and 25-28).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to use lentogenic NDV in the method of treating cancer in a patient. As a matter of designer's choice, one of ordinary skill in the art would have been motivated to use lentogenic NDV as the NDV in the method because lentogenic NDV is a low virulence strain as exemplified by Roberts (page 7).

In addition, at the time the invention was made, one of ordinary skill in the art understands that EID50 per unit does, EID50/cell and pfu were common units for determining virus concentration. In addition, the range taught by Roberts is an obvious variant on the concentration recited in instant claims 29 and 30.

With respect to the limitation directed to dosage of NDV used in the claimed method.

MPEP 2144.05 recites: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). This is the case here. The specification (page 3) does not disclose that the limitation in instant claims 29-30 is critical for one of ordinary skill in the art to practice the claimed invention.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use 10^6-10^{12} EID_{50} per unit dose of HUJ strain of NDV or in a range of 20 EID_{50}/cell to 2000 EID_{50}/cell in the method. One of ordinary skill in the art would have been motivated to use either range because the range taught by Roberts is an obvious variant of the limitations in instant claims 29 and 30 and one of ordinary skill in the art would make the necessary modifications to the dosage to practice the claimed method.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5733556 and 5762938 teach using a composition comprising NDV comprising EID50. However, both patents are directed to using NDV as a vaccine for producing antibodies against NDV and not for killing tumors.

SEQ ID NO: 1 in instant claim 1 is free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman
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